Epithelioid Angiosarcoma Presenting as a Huge Cystic Mass in the Right Hemithorax: A Rare Case Report and Diagnostic Pitfall

Tanyasorn Sutthipongsupa
Department of Anatomical Pathology, Chonburi Hospital, Chonburi Province, Thailand

Article info: Received: October 27, 2025 | **Revised:** November 17, 2025 | **Accepted:** November 28, 2025

Abstract

Epithelioid angiosarcoma (EAS) is a rare, highly aggressive vascular malignancy arising from endothelial cells, characterized by variable morphology and challenging diagnosis. Involvement of the chest wall or hemithorax was uncommon and posed diagnostic difficulties due to morphological heterogeneity and overlap with other epithelioid tumors. This case report described the clinical and histopathological features of a malignant vascular tumor occurring in the right hemithorax. Clinical data were collected from electronic medical records using the electronic public health information system (e-Phis) of Chonburi Hospital. The patient was a 42-year-old man who presented with right-sided chest pain and pleural effusion. Imaging revealed a large cystic and hemorrhagic lesion occupying the right hemithorax. The initial thoracotomy specimen demonstrated a fibrous-walled pseudocyst with organized hematoma and calcification, without evidence of malignancy. After a two-year follow-up, repeat biopsy revealed epithelioid cells with abundant amphophilic cytoplasm, vesicular pleomorphic nuclei, and prominent nucleoli, accompanied by hemorrhage, necrosis, and high mitotic activity. Immunohistochemistry showed diffuse positivity for CD31, CD34, FLI-1, AE1/AE3, Vimentin, and cytoplasmic WT1, and negativity for D2-40, calretinin, SALL4, and TTF-1, confirming high-grade EAS. After diagnosis, the patient deteriorated rapidly, and he died despite aggressive management. This case highlighted the diagnostic pitfalls of EAS presenting as a benign-appearing cystic lesion. Initial sampling may have miss the malignant component, delaying diagnosis. Thorough histopathological evaluation, repeat biopsy, and comprehensive immunohistochemistry were essential to distinguish EAS from morphologically similar epithelioid neoplasms. Early recognition and prompt pathological diagnosis were crucial, but prognosis remained poor even with aggressive management.

Keywords: Epithelioid angiosarcoma, Hemithorax, Immunohistochemistry, Case report

Corresponding Author: Tanyasorn Sutthipongsupa **Email:** tanyasornnick@gmail.com

Phetchabun Medical Journal
Vol.5 No.3 September-December 2025

แองจิโอซาร์โคมาชนิดอิพิทีลิออยด์ที่แสดงออกเป็นก้อนซีสต์ขนาดใหญ่ในครึ่งทรวงอกขวา: รายงานผู้ป่วย 1 ราย และหลุมพลางการวินิจฉัย

ธัญญาสรณ์ สุทธิพงษ์สุภา
กลุ่มงานพยาธิวิทยากายวิภาค โรงพยาบาลชลบุรี

การรับบทความ: วันที่รับ: 27 ตุลาคม 2568 | **วันที่แก้ไข:** 17 พฤศจิกายน 2568 | **วันที่ตอบรับ:** 28 พฤศจิกายน 2568

บทคัดย่อ

แองจิโอซาร์โคมาชนิดอิพิทีลิออยด์ (Epithelioid angiosarcoma, EAS) เป็นเนื้องอกหลอดเลือดชนิดร้ายที่พบได้ยาก มีต้นกำเนิดจากเซลล์บุผนังหลอดเลือด และมักมีลักษณะทางจุลพยาธิวิทยาแปรผัน ทำให้วินิจฉัยได้ยาก การเกิดที่ผนังทรวงอกหรือครึ่งทรวงอกพบได้น้อยและมักสร้างความยากลำบากในการวินิจฉัย รายงานผู้ป่วยนี้มีวัตถุประสงค์เพื่อนำเสนอลักษณะทางคลินิกและจุลพยาธิวิทยาของเนื้องอกหลอดเลือดชนิดร้ายที่เกิดขึ้นในครึ่งทรวงอกขวา ข้อมูลทางคลินิกของผู้ป่วยถูกเก็บรวบรวมจากเวชระเบียนอิเล็กทรอนิกส์ โดยใช้ระบบสารสนเทศสาธารณสุขอิเล็กทรอนิกส์ (e-Phis) ของโรงพยาบาลชลบุรี ผู้ป่วยเป็นชายอายุ 42 ปี มีอาการปวดชายโครงขวาและมีน้ำในช่องเยื่อหุ้มปอด ภาพรังสีพบก้อนถุงน้ำขนาดใหญ่และมีเลือดออกซึ่งกินพื้นที่ภายในทรวงอกด้านขวา ชิ้นเนื้อจากการผ่าตัดเปิดทรวงอกครั้งแรกพบถุงน้ำเทียมที่มีผนังเป็นเนื้อเยื่อพังผืดร่วมกับก้อนเลือดเก่าและมีการสะสมของหินปูนโดยไม่มีหลักฐานของเนื้องอกร้าย หลังติดตามผู้ป่วย 2 ปี การตรวจชิ้นเนื้อซ้ำแสดงให้เห็นเซลล์ชนิดอิพิทีลิออยด์ซึ่งมีไซโทพลาซึมชนิดแอมโฟฟิลิกในปริมาณมาก มีนิวเคลียสที่โป่งพองและมีหลายรูปแบบ และมีนิวคลีโอลัสเด่นชัด ร่วมกับมีภาวะเลือดออก เนื้อตาย และอัตราการแบ่งตัวสูง ผลย้อมภูมิคุ้มกันพบ CD31, CD34, FLI-1, AE1/AE3, Vimentin และ WT1 (ติดไซโตพลาซึม) แต่ไม่พบ D2-40, calretinin, SALL4 และ TTF-1 ซึ่งสนับสนุนการวินิจฉัย EAS ชนิดร้ายระดับสูง แม้จะได้รับการรักษาอย่างเข้มข้น ผู้ป่วยได้มีอาการทรุดลงและเสียชีวิตหลังจากได้รับการวินิจฉัย 3 เดือนต่อมา กรณีศึกษานี้ได้เน้นย้ำถึงประเด็นที่ต้องระวังในการวินิจฉัย EAS ซึ่งแสดงลักษณะเป็นรอยโรคถุงน้ำที่ดูไม่ร้ายแรง การเก็บตัวอย่างชิ้นเนื้อครั้งแรกอาจพลาดส่วนประกอบที่เป็นเนื้อร้าย ทำให้การวินิจฉัยล่าช้า การประเมินทางจุลพยาธิวิทยาอย่างละเอียด การตรวจชิ้นเนื้อซ้ำ และการย้อมภูมิคุ้มที่ครอบคลุม จึงมีความจำเป็นอย่างยิ่งในการแยก EAS ออกจากเนื้องอกชนิดอิพิทีลิออยด์ที่มีรูปร่างคล้ายคลึงกัน การรับรู้ตั้งแต่ระยะเริ่มต้นและการวินิจฉัยทางพยาธิวิทยาที่รวดเร็วนั้นมีความสำคัญอย่างยิ่ง แต่อย่างไรก็ตาม ผลการพยากรณ์โรคก็ยังคงไม่ดี แม้จะมีการรักษาที่เข้มข้นก็ตาม

คำสำคัญ: แองจิโอซาร์โคมาชนิดอิพิทีลิออยด์, ครึ่งทรวงอก, อิมมูโนฮิสโตเคมี,รายงานผู้ป่วย

ผู้รับผิดชอบบทความ: ธัญญาสรณ์ สุทธิพงษ์สุภา **Email:** tanyasornnick@gmail.com

Introduction

Epithelioid angiosarcoma (EAS) is a rare, high-grade vascular sarcoma arising from endothelial cells, representing about 20–30% of all angiosarcomas. Although it can occur in various organs, involvement of the chest wall or pleura is uncommon. [1] Primary EAS arising in the pleura or hemithorax is exceedingly rare, with fewer than 50 cases reported in the literature [2,3]. Despite its predominantly sporadic nature, the disease has been reported in association with radiation therapy, chronic lymphedema, or chemical carcinogen exposure [1, 4-5].

Diagnosis is challenging due to its variable morphology and overlap with other epithelioid neoplasms such as mesothelioma and metastatic carcinoma. Histopathological evaluation plays a pivotal role in establishing the diagnosis. Hematoxylin and eosin (H&E) staining typically reveals epithelioid endothelial cells with abundant eosinophilic or amphophilic cytoplasm, prominent nucleoli, and vasoformative features. However, when only a small number of tumor cells are present, these atypical cells may be easily overlooked on routine examination. Therefore, immunohistochemistry plays a crucial role in establishing the diagnosis and distinguishing EAS from morphologically similar tumors [1,6–8], as the tumor cells typically express endothelial markers such as CD31, CD34, ERG, and FLI-1, while lacking epithelial markers such as cytokeratin.

EAS carries a poor prognosis, with a median survival of less than six months [4]. To our knowledge, there have been no previously reported cases of EAS involving the chest wall or right hemithorax in Thailand. This case is notable for its unusually large cystic presentation, initially mimicking a benign lesion and posing diagnostic challenges. Herein, we report a rare case of EAS presenting as a huge cystic lesion in the right hemithorax, diagnosed in Chonburi province, Thailand. The purpose of this case report is to describe the clinical and histopathological characteristics of EAS occurring in the right hemithorax, with the goal of enhancing diagnostic accuracy for this tumor in an uncommon location.

Case Presentation

A 42-year-old male with no comorbidities presented with persistent right-sided chest pain for 2 weeks and a mild cough without fever. Physical examination revealed diminished breath sounds, decreased vocal resonance, and percussion dullness over the right lung. He was admitted for further investigation to determine the underlying cause. Clinical data were retrieved from the electronic medical records of Chonburi Hospital using the e-Phis system. Chest radiograph showed a massive right pleural effusion with mediastinal shift. Computed tomography (CT) revealed a large heterogeneous lesion (11.3 × 15.0 × 23.4 cm) with thick rim enhancement, calcifications, mixed densities, and air pockets, resulting in volume loss of the right hemithorax (Figure 1). Pleural tapping for pleural fluid analysis was performed and demonstrated a complicated parapneumonic

effusion with a white blood cell count of 5,500/μL (70% neutrophils), a glucose level of 11 mg/dL, and negative culture results.

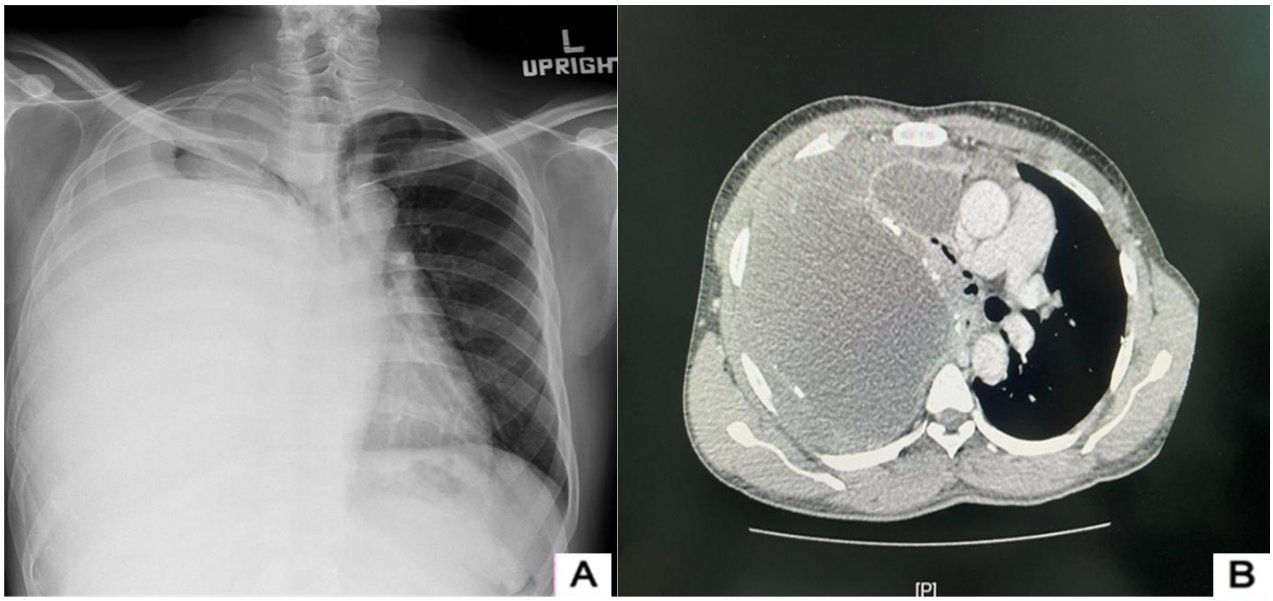

Figure 1. (A) Chest radiograph showing a massive right pleural effusion with marked mediastinal shift. (B) Axial contrast-enhanced CT demonstrating an irregular heterogeneous mass with thick rim enhancement occupying the right hemithorax.

The patient subsequently underwent a thoracotomy with tumor removal. Histopathologic examination of the surgical specimen revealed a fibrous-walled pseudocyst with organized hematoma and focal calcification. Postoperative recovery was uneventful, and follow-up visits were scheduled twice yearly.

Two years later, the patient was readmitted with exertional dyspnea and shortness of breath. He was diagnosed with a complicated parapneumonic pleural effusion and underwent a modified Eloesser flap for drainage, debridement, and biopsy. Histopathologic evaluation using hematoxylin and eosin staining (H&E) demonstrated epithelioid cells with abundant amphophilic cytoplasm, pleomorphic vesicular nuclei, and prominent nucleoli. The cells formed vasoformative patterns with anastomosing channels and were accompanied by hemorrhage, approximately 20% necrosis, and a mitotic rate of 7 mitoses per 10 HPFs (7/10 HPFs) (Figure 2). Immunohistochemistry revealed diffuse positivity for CD31, CD34, FLI-1, AE1/AE3 (focal), cytoplasmic WT1, and vimentin, whereas the tumor cells were negative for D2-40, calretinin, SALL4, and TTF-1 (Figure 3). These findings were consistent with a diagnosis of high-grade epithelioid angiosarcoma (EAS).

To investigate a potential relationship between the previously resected pseudocyst and the subsequent development of epithelioid angiosarcoma, the original microscopic slides were retrieved for diagnostic reevaluation. Retrospective examination of the entire

slide set revealed minute foci of atypical cells (<1 mm) that had been inconspicuous in the initial assessment, explaining for the missed diagnosis in the first evaluation. (Figure 4)

After the modified Eloesser flap procedure, a small amount of pleural fluid still remained, and the patient developed progressive malaise and exertional dyspnea. During follow-up, he required supportive care, including hospitalization for correction of dehydration and electrolyte imbalance, management of deteriorating functional status and dyspnea, and treatment of infectious complications as they arose. He did not receive chemotherapy or radiotherapy. Ultimately, his condition deteriorated rapidly, and he died three months after the diagnosis.

Discussion

The present case illustrates a significant diagnostic challenge because the initial pathological examination revealed only a fibrous cyst wall with organized hematoma and calcification, without clear evidence of malignancy. Such a histologic pattern can mimic a chronic inflammatory or post-traumatic lesion and may delay recognition of an underlying tumor. The paucity of atypical cells in the initial specimen may have obscured the diagnosis of sarcoma, particularly a vascular malignancy such as epithelioid angiosarcoma. A definitive diagnosis was achieved only after a repeat biopsy demonstrated more overt malignant epithelioid cells.

Nevertheless, the morphology in such cases can overlap with several other entities, thereby broadening the differential diagnosis. Metastatic carcinoma is often the first consideration when epithelioid malignant cells are identified, especially if they express cytokeratin. However, the lack of specific organ-related markers and the strong expression of endothelial markers such as CD31, CD34, and FLI-1 in this case supported a vascular origin rather than carcinoma [6, 9-11]. Another important consideration is malignant mesothelioma, particularly when the lesion arises in the pleural or hemithoracic cavity. Mesothelioma typically expresses calretinin and D2-40 and shows nuclear staining for WT1, while endothelial markers are negative. In this case, the absence of these mesothelial markers, combined with diffuse positivity for endothelial markers, effectively excluded mesothelioma [1,10]. Epithelioid hemangioendothelioma (EHE) also enters the differential diagnosis because of its epithelioid morphology and expression of endothelial markers. However, EHE usually exhibits a lower grade with less cytologic atypia, a lower mitotic rate, and lacks the extensive necrosis observed in this case. Furthermore, EHE characteristically harbors a WWTR1 – CAMTA1 fusion, which distinguishes it from EAS [4,6,9]. An additional theoretical consideration is angiosarcoma arising in a teratoma, particularly when calcifications and fibrous cyst walls are present, as in this case. Teratomas typically contain components derived from multiple germ layers, and angiosarcoma may arise as a malignant transformation within teratomatous tissue [4, 12-13]. Despite the presence of calcifications

and fibrous walls, repeated sampling in this case failed to reveal any teratomatous elements, and the tumor was negative for SALL4, making a germ cell tumor unlikely.

Immunohistochemistry played a crucial role in establishing the final diagnosis. The tumor cells expressed CD31, CD34, FLI-1, vimentin, and AE1/AE3, confirming their endothelial differentiation despite the co-expression of cytokeratin, which could have suggested carcinoma. The lack of staining for D2-40, calretinin, and nuclear WT1 excluded mesothelioma, while negative SALL4 and TTF-1 staining ruled out germ cell tumor and lung carcinoma, respectively. These findings further support the diagnosis of EAS.

In the absence of identifiable risk factors, the tumor in this case likely represents a de novo EAS rather than secondary transformation from a pre-existing lesion. This highlights the importance of considering EAS even in patients without apparent risk factors, particularly when confronted with atypical cystic or hemorrhagic thoracic lesions.

Conclusion

This case illustrates the diagnostic difficulty of epithelioid angiosarcoma (EAS) of the right hemithorax, initially masked by benign-appearing fibrous tissue, hematoma, and calcification. The diagnosis was confirmed only after repeat tissue sampling and immunohistochemical analysis. It underscores the importance of adequate tissue sampling, recognition of subtle morphological atypia, and careful immunohistochemical evaluation to distinguish EAS from other epithelioid malignancies. In clinical practice, when a pathologist encounters a pseudocystic lesion in the hemithorax, extensive tissue sampling and meticulous examination for areas of atypical cells within the cyst wall are recommended. This approach enables appropriate immunohistochemical evaluation and optimizes diagnostic accuracy in rare thoracic vascular tumors, as illustrated in this case.

Acknowledgment

The author gratefully acknowledges Kaywalin Sutthipong, MD, for her valuable radiological consultation, and sincerely thanks Jirawat Chuaykaew, MD, for his kind encouragement and continuous support throughout the preparation of this case report.

Disclosure of conflicts of interest

The authors declare that there are no conflicts of interest regarding the research, authorship, or publication of this article.

Ethical Considerations and Patient Confidentiality

This study involved the retrospective use of anonymized medical record data. Patient confidentiality was strictly protected, and all personally identifiable information was removed prior to analysis. Only the principal investigator had access to the dataset, which was used solely for academic and research purposes.

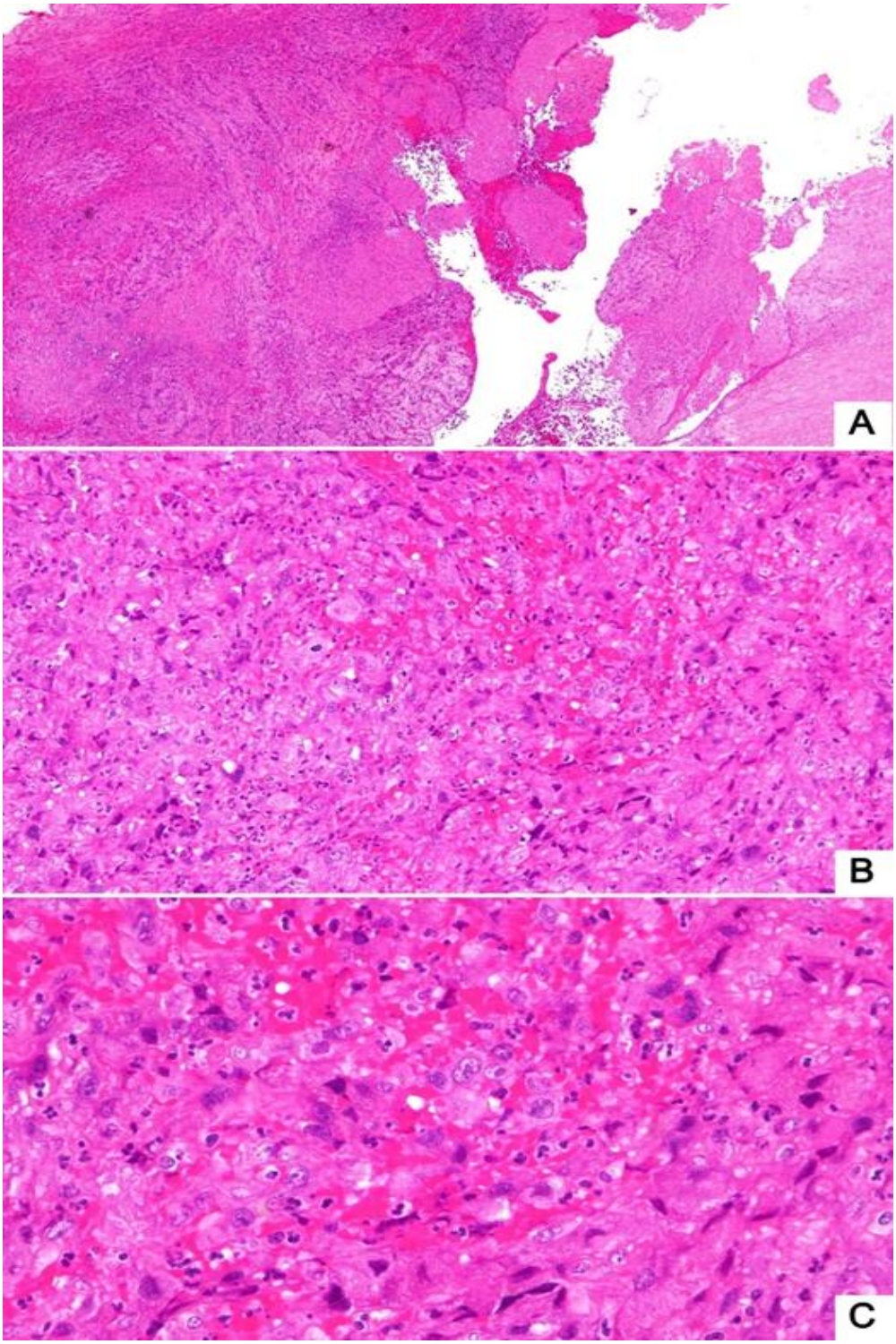

Figure 2. Histologic features (H&E) showing a thick fibrotic wall containing hemorrhagic tissue and fibrin (A, ×40). High-magnification examination demonstrates infiltration by atypical epithelioid cells (B, ×200), which appear discohesive and exhibit hyperchromatic, pleomorphic and vesicular nuclei and abundant amphophilic cytoplasm. Some cells show prominent nucleoli (C, ×400).

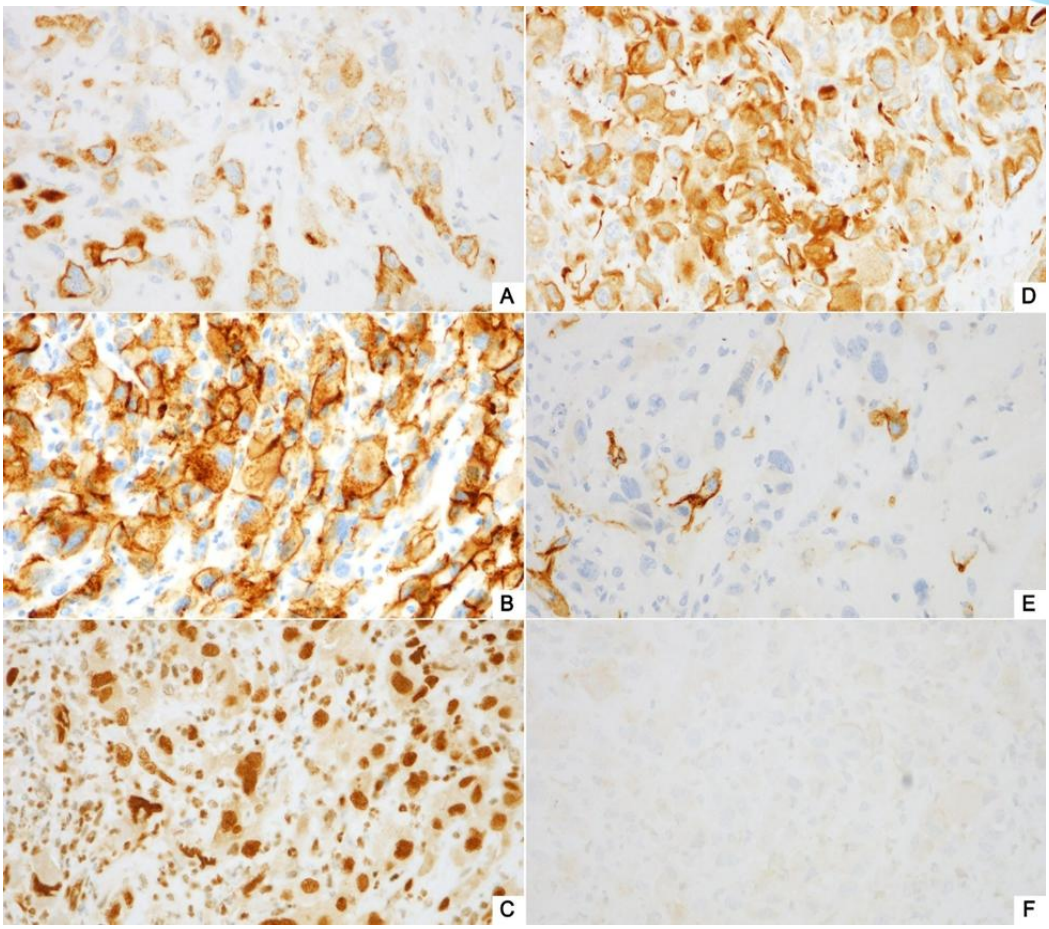

Figure 3. Immunohistochemical studies demonstrating positivity for cytokeratin (AE1/AE3) (A), CD31 (B), FLI-1 (C), WT1 (D), CD34 (E), with negativity for SALL4 (F) (A-F, ×400).

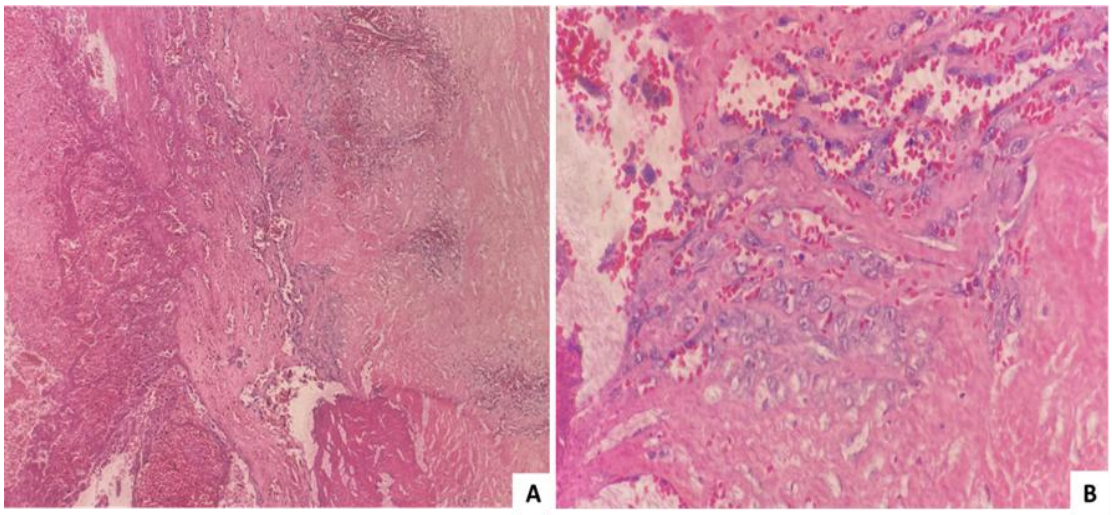

Figure 4. Histopathologic features (H&E) of the cystic lesion. Low-power view shows a fibrotic-walled pseudocyst containing organizing hematoma and focal calcification (A, ×40). High-power view demonstrates small foci of atypical epithelioid cells (<1 mm), which were initially inconspicuous on retrospective review (B, ×200).

References

[1.] Fan C, Liu Y, Lin X, Han Y, He A, Wang E. Epithelioid angiosarcoma at chest wall which needs to be carefully distinguished from malignant mesothelioma: report of a rare case. Int J Clin Exp Pathol. 2014;7(12):9056–9060.

[2.] Zhang S, Zheng Y, Liu W, Yu X. Primary epithelioid angiosarcoma of the pleura: a case report and review of literature. Int J Clin Exp Pathol. 2015;8(2):2153–2158.

[3.] Yavuz H, Tekneci AK, Akcam TI, Turhan K, Akalın T. Pleural angiosarcoma presenting with spontaneous hemothorax. Indian J Thorac Cardiovasc Surg. 2023;39(5):543–546.

[4.] Weissferdt A, Kalhor N, Suster S, Moran CA. Primary angiosarcomas of the anterior mediastinum: a clinicopathologic and immunohistochemical study of 9 cases. Hum Pathol. 2010;41(12):1711–1717.

[5.] Tan YB, Yu XF, Fan JQ, Li JF. Angiosarcoma originating in the anterior mediastinum: a case report. Medicine (Baltimore). 2018;97(50):e13459.

[6.] Hart J, Mandavilli S. Epithelioid angiosarcoma: a brief diagnostic review and differential diagnosis. Arch Pathol Lab Med. 2011;135(2):268–272.

[7.] Ko JS, Billings SD. Diagnostically challenging epithelioid vascular tumors. Surg Pathol Clin. 2015;8(3):331–351.

[8.] Panjwani A, Singh I, Parvataneni N, Talukdar P. Spontaneous hemothorax: primary pleural epithelioid angiosarcoma. Egypt J Intern Med. 2016;28:170–173.

[9.] Cheng X, Yang G, Liu J, Liu F. Epithelioid angiosarcoma of the chest wall with atypical morphology: report of one case. Int J Clin Exp Pathol. 2019;12(10):3944–3948.

[10.] Paral K, Krausz T. Vascular tumors of the mediastinum. Mediastinum. 2020;4:25.

[11.] Zhang Y, Huang X, Peng C, Wang Y, Wu Q, Wu Z, et al. Primary pulmonary epithelioid angiosarcoma: a case report and literature review. J Cancer Res Ther. 2018;14(Suppl):S533–S535.

[12.] Contreras AL, Punar M, Tamboli P, Tu SM, Pisters L, Moran C, et al. Mediastinal germ cell tumors with an angiosarcomatous component: a report of 12 cases. Hum Pathol. 2010;41(6):832–837.

[13.] Acharya S, Pokima N, Yetiskul E, Achkar M, Grabie YY, Khanijo S, et al. Teratoma to angiosarcoma: a metamorphosis in the mediastinum. Cureus. 2024;16(6):e62555.